in all. In four with nephrosis, proteinuria fell from more than 8g. per 24 hrs to less than 0.5g. per 24 hrs in three, and 2g. per 24 hrs in the fourth, with return to normal of serum albumin concentration. Two of these patients agreed to a second renal biopsy which showed a significant reduction in cellular infiltration. In the fifth patient renal function deteriorated, necessitating dialysis, but during treatment with chlorambucil creatinine clearance improved from less than 10 to 62 ml./min. The disease remains quiescent in all after 5, 5, 4, 2, and 1½ years. The sixth patient was treated with chlorambucil because corticosteroids alone had failed to keep her peripheral vascular manifestations under control. She remains well 4 years afterwards.

No adverse effect from treatment has yet occurred in these patients, but there is an increasing unease concerning the risk of malignant disease in patients undergoing immunosuppressive therapy. In an investigation into chromosomal abnormalities associated with chemotherapeutic drugs, abnormalities have been observed after cyclophosphamide, but so far not in patients taking chlorambucil.

Discussion

DR. H. L. F. CURREY (*London*) Have you encountered any herpes zoster? Kahn and de Sèze (1971) have most experience with this drug in rheumatoid arthritis and they found a very high incidence of herpes zoster. Interestingly, they suggest that there is a correlation between the clinical response and the incidence of herpes zoster.

DR. SNAITH There was one patient who had this condition but she developed it before she started chlorambucil.

A PHYSICIAN: Did you monitor the serum complement or DNA binding and were you able to show any changes?

DR. SNAITH At the time the DNA binding was not available, but we did look at the complement. This was rather variable and, as the results went back over nearly 10 years, we feel rather doubtful about the reliability of the test. Sometimes it was low and sometimes it was normal.

DR. K. T. RAJAN (*Cardiff*) In view of the teratogenic action ascribed to the drug, did you look at the infant of one of your patients who delivered soon after starting treatment?

DR. SNAITH Yes, we looked and the infant was normal.

Reference

Kahn, M.-F., and Sèze, S. de (1971) 'INSERM Colloque', Hôpital Cochin (Paris) 3-5 November (Polyarthrite chronique rhumatoïde et immunodépression)

Effect of Weight Reduction on Levels of Uric Acid in Plasma and Urine.* By A. NICHOLLS, H. YABLONSKY, and J. T. SCOTT (*West London Hospital and Kennedy Institute of Rheumatology*)

There is now considerable evidence of a relationship between body weight and plasma urate levels. Such an association has been found in epidemiological surveys (Healey and Hall, 1970) and many gouty patients tend to be overweight (Grahame and Scott, 1970). The nature of this association is unknown. The present study was designed

to determine whether weight reduction in individuals has any effect on plasma and urinary urate.

Fifteen subjects were studied, 10 men (5 of them with untreated hyperuricaemia and gout) and 5 women (one with hyperuricaemia). Three 24-hr urate and creatinine clearance estimations were made on a low-purine diet before and after a period of weight reduction.

Mean weight loss was 8 kg. (range 4 to 22). In 12 of the 15 subjects, the plasma urate fell, and in the group as a whole this was significant (mean fall 0.8 mg./100 ml.; $P < 0.01$). There was no consistent change in urinary urate levels (mean fall 82 mg./24 hours; not significant), although four subjects with the highest urinary levels showed a marked fall after weight loss. Creatinine clearance remained unchanged.

The results show clearly that weight reduction produces a fall in plasma urate and therefore suggest that plasma urate levels are influenced by body weight. The mechanism of this fall in urate remains uncertain; a decrease in urinary urate seen in some subjects may mean that urate production is diminished, but this was not a consistent finding and it is possible that other additional (*i.e.* renal) factors may be operating. Total body water is relatively greater after weight loss, which may be a factor in producing a lower level of uric acid in the plasma.

Discussion

DR. B. D. OWEN-SMITH (*Reading*) I should like to confirm these findings. We placed four obese males on alternate 15-day periods of fasting followed by 15 days re-feeding with a low purine metabolic diet, for a total of 60 days. Weight loss (25 kg. average) was similar for all subjects. Hyperuricaemia recurred during fasting and was corrected by re-feeding. There was a fall in the average and peak serum uric acid levels with successive fasts and also in the average and basal levels with successive feeding periods. There was no significant change in renal function as measured by creatinine clearance during the study to account for the fall in serum uric acid level with weight loss.

DR. J. D. GOODE (*Hull and East Riding*) Have you any information on alcohol intake before and after the period of weight reduction?

DR. NICHOLLS These patients were all on a low purine, alcohol-free diet at the time of urine collections, and for a week before, so this should not have affected our results.

DR. J. MATTHEWS (*London*) It would be helpful in assessing the degree of hyperuricaemia if we know the upper limit of normal of your laboratory. You also did not tell us whether you actually observed a reduction in the number of gouty attacks.

DR. NICHOLLS The six patients that we were studying with gout were not, in fact, having treatment at the time because the attacks were infrequent. They did not have any attacks during the time they were losing weight but the numbers were too small to draw any conclusions.

DR. SCOTT The mean value of plasma uric acid in our laboratory for normal adult men on a low-purine diet is 5.1 mg./100 ml. with a standard deviation of 1.0, so that you could define the upper limit as about 7.0 mg./100 ml. This is not really relevant to the present study, however, since we are concerned with changes in particular indi-

* A more detailed account of this work has been published in the *Lancet* (1972) 2, 1223

viduals. Fall in plasma urate with weight loss occurred in both hyperuricaemic gout patients and normal subjects.

PROF. E. G. L. BYWATERS (*Taplow*) Do you have any plans to follow up these people during the periods of stabilization and reversion to normal, because this again would give very valuable data?

DR. NICHOLLS We hope to carry on observing them.

DR. R. GRAHAME (*London*) You may have influenced the excretion of uric acid into the gastrointestinal tract. Did you consider this?

DR. NICHOLLS We have no data on that possibility.

DR. B. D. OWEN-SMITH We recently demonstrated in one subject a significant increase in uric acid elimination *via* the gut in hyperuricaemia due to fasting, confirming the findings of Sorensen (1960) of increased intestinal uricolysis in hyperuricaemia.

References

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